Harnessing the power of bioelectronics and instrumentation: Need for integrated approach and skill development for innovation

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Abstract: *In the era of globalization there is a continuous demand for better quality of life. Dynamic and diverse nature of unmet needs of society dictates us to be innovative in different fields. Science, engineering and technology research is the strong driving force of innovations which helps us to tackle the global and societal challenges we face. Innovations support the wealth and welfare of the nation and contribute to the progress of any country. They are the growth engines for knowledge driven economy. The field of bioelectronics has seemingly endless innovation possibilities because of its potential for developing new and exciting applications that address the needs of society and scientific community. Bioelectronics is an interdisciplinary research area that deals and integrates the technical ability of electronics, electrical engineering principles for application of biological, medical and health solutions. It deals with development of sophisticated and robust detection technologies for development of a broad range of functional innovative bio and medical electronic devices. Such devices include recognition or sensing devices such as biosensors, electronic aids for human senses , biochips, blood pressure and flow monitors, electrocardiographs, cardiac pacemakers, implantable sensor, molecular motors, defibrillator and various medical imaging systems . A variety of bioelectronic devices are reported in the market and literature at various stages of discovery, development and commercial stages, however products are relatively costly and the market is dominated by western countries, North America in particular. In terms of global bio-electronics market size, value, patents and innovations, India's share is relatively minimal, in spite of technological advancements in various fields. This paper tries to provide an insight into the topic, tries to stimulate and nucleate interdisciplinary ideas. It further emphasizes the need for interdisciplinary research and integrated approach, promoting, managing intellectual properties, skill and entrepreneurship development for harnessing the potential of bioelectronics.*

Introduction

Bioelectronics is an interdisciplinary research area resulting from the convergence of biology and electronics that explores the power electronics, electrical engineering principles for application of biological, medical and health solutions. Bio-chips, Implantable medical devices, Prosthetic devices, artificial organs and electronic pills are some of the applications. Electronic devices have been revolutionizing biology and medicine over the past several generations. It is also considered to be next medical frontier with great potential to significantly impact healthcare and medicine (Omprakash 2016 Alyssa 2016). Quality of life has increased with the advances in medical technology. Power electronics had an impact on further development and digitalization of medical devices and improving precision. Significant improvements and advances are seen in thermometers, stethoscope, ophthalmoscope, laryngoscope, electrocardiography, scanning technologies, and medical imaging and medical implants. Such advances include graphically display of the sounds and using techniques such as voiceprint analysis for diagnosis and

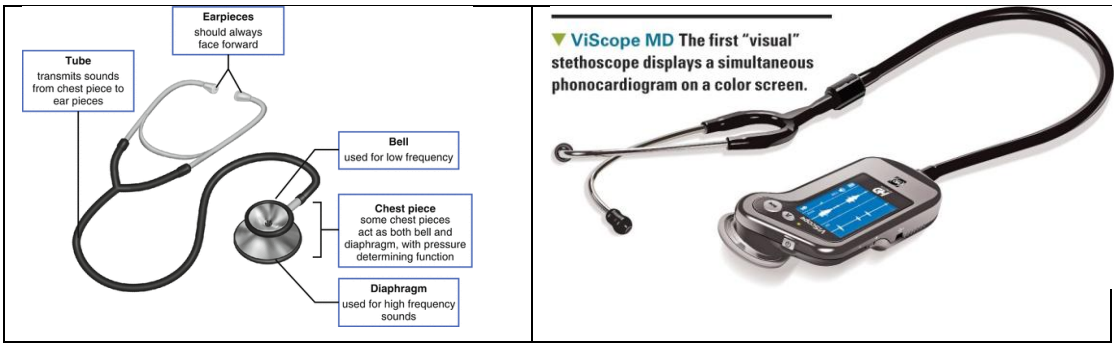
monitoring. As per envision market report global Bio-Electronics market is valued at $13.75billion in 2018 and estimated to reach a value of $27.25billion in 2024 at CAGR of 13.76% (Htf market report 2018 ,Nic Lempriere-Hogg 2017). An overview of improvements and advances in selected promising medical devices along market literature information and patents relevant to bioelectronics and instrumentation for innovation is presented below. A careful analysis of such relevant patents dictate the need for interdisciplinary research will nucleate ideas for innovation.

Stethoscopes

Stethoscope was considered to be one of the important and earliest medical diagnostic devices that allow physicians to listen to the sounds of lungs and heartbeats of patients and relate them to functioning and malfunctioning organs. Chest Piece, Tubing, Ear Pieces are the main components of this medical device. In brief sound is transmitted from the chest piece which consists of two parts bell which transmits lower frequency sounds and diaphragm transmits higher frequency sounds through the air-filled hollow tubes to ears. Digital stethoscopes offer sophisticated capabilities, such as audio recording and playback, and provide data to visually chart results by connecting to an off-instrument display. The essential elements of a digital stethoscope are the sound transducer, the audio codec electronics, and the speakers. The sound transducer is the most critical piece in the chain. It determines the diagnostic quality of the digital stethoscope. According to a market research analysis report: The global stethoscope market size was valued at USD 327.7 million in 2016 and is expected to grow at a CAGR of 4.7% .America dominates the global stethoscopes market accounting for more than 46% of the market followed by European market contributing close to 34% (Grand view research report 2017) Market data, patent and literature indicate there is an opportunity for innovation

Following are relevant interesting US patents on digital stethoscope

PAT. NO.	Title
9,848,848	Lung sound denoising stethoscope, algorithm, and related methods
9,572,521	Monitoring biometric characteristics of a user of a user monitoring apparatus
9,566,041	Adhesive patch having multiple acoustic sensors for monitoring acoustic signals
9,301,032	Stethoscope chestpiece usable with a portable electronic device and related methods
5,841,846	Digital telephonic system for stethoscope signal processing



	
Conventional Stethoscope	Modern electronic Stethoscope

Figure 1: Picture depicting Innovation in digitalization on stethoscope
Source: https://link.springer.com, http://students.iitk.ac.in/projects

Blood pressure monitors

Blood pressure is a measure of the pressure of circulating blood on the walls of blood vessels. Millions of patients visit their doctors yearly to monitor and control their blood pressure and is integral part of clinical practice. High blood pressure worldwide is considered as a contributing risk factor for cardiovascular disease which is responsible for around 12.8 percent of all global deaths. Blood pressure is traditionally measured by a **sphygmomanometer**, also known as a blood pressure monitor or meter. It consists of an inflatable cuff generally applied to the arm which helps to collapse and release arteries in a controlled manner and a mechanism for inflation usually a manually operated bulb or an electronically operated pump. It is and connected to a column of mercury next to a graduated scale, enabling the determination of systolic and diastolic blood pressure by increasing and gradually releasing the pressure in the cuff. Manual sphygmomanometers are usually used in conjunction with a stethoscope. Fast and accurate blood pressure reading is essential and could be a matter of life and death in a professional critical medical care, emergency or hospital setup. Cost, ease of use and problems of mercury lead to many innovations and development of Blood pressure monitors which accurately measure blood pressure and pulse rate. Present day digital BP monitors vary in price are portable, convenient and give quick and accurate readings. Digital monitoring instruments may use a cuff placed, fitted on the wrist, worn around the upper arm, or a finger. They employ deformable membranes and microprocessors that estimate differential capacitance. In digital BP monitors the cuff is inflated and released by an electrically operated pump and valve. Innovations are leading to use of Wireless technology is being used to transmit data digital blood pressure monitors to remote locations, for better interface and maintenance of electronic medical records. Smartphone compatible blood pressure monitors are developed. There is further great scope for developing medical electronic devices called vital signs monitors integrating blood pressure measurement with other vital signs such as temperature, pulse, and SpO2.These modern medical electronic devices are in use currently used in advanced medical care hospitals and clinics. However are very costly add up the critical care health cost (Jose et al, 2018)

Following are relevant US patents on digital blood pressure measurement devices

PAT. NO.	Title
9,649,054	Blood pressure measurement method
9,532,722	Patient monitoring system
9,289,139	Blood pressure monitor

7,607,431	Medical reminder device suited for use with nebulizers
6,893,401	Continuous non-invasive blood pressure monitoring method and apparatus

Manual Blood Pressure Monitor

Digital Blood Pressure Monitors

Figure 2: Picture depicting Innovation in digitalization of Blood Pressure Monitor
Source:https://b2bbusinessnews.wordpress.com/2013/03/01/comparison-between-manual-and-digital- blood-pressure-monitors/

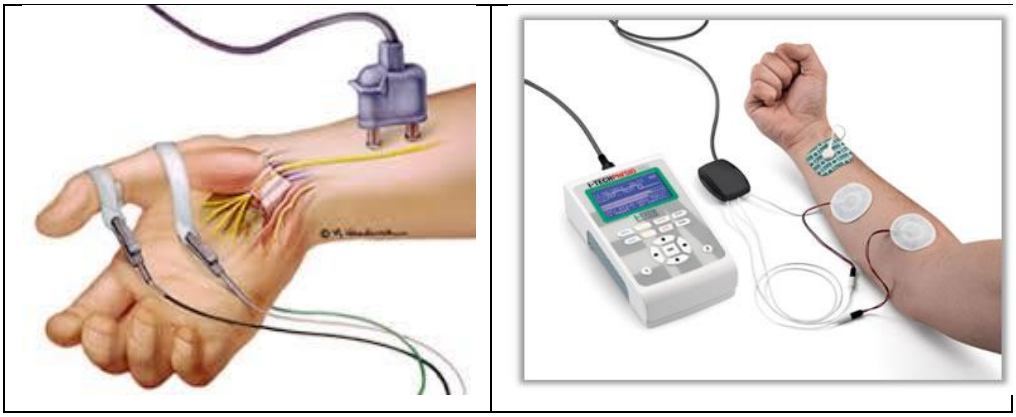
Electrophysiological instrumentation.

Understanding of bioelectricity, low level electrical currents associated with mammalian cells, organs, and organisms has led to the development of electrophysiological instrumentation. **Electrocardiography (ECG/EKG**) is based on biophysical principle involving trapping, amplifying and recording micro electrical signals of the heart by means of electrodes stick to the skin and recorded by a device external to the body. It is used to quickly diagnose and monitor events before and after life-threatening and rhythm disorders of the heart. Developments in Einthoven's original string galvanometer led to modern EKG instrument. Electronic features such as computing hardware and software algorithms are incorporated in these medical electronic devices that identify life-threatening arrhythmias and provide sound alarms so that immediate urgency therapeutic measures can be taken. Cardiac monitor displays the ECG in real time is an advanced medical electronic device for observing the ECG in critical care situations and in cardiac rhythm disorders. Electrocardiograph and related cardiac patient monitors are important parts of now an integral part of clinical practice (Burch & DePasquale 1990). Hand held echocardiography systems offer many advanced advantages in examining the patients over stethoscopes. Developments in handheld echocardiography technology capable of depicting 3D cardiac video images of normal echocardiograms are of paramount importance for training medical professionals for enhanced the accuracy of physical diagnosis (Dave Fornvell 2015).

Conventional and new generation of ECG systems

Figure 3: Picture depicting a new generation of ECG systems that integrate touch screen monitors
Source: Advances in ECG Technology | DAIC SEPTEMBER 16, 2015

Similarly Electromyography (EMG) measures electrical activity of muscle at rest and during contraction using oscilloscope and display it in the form of waves on and a monitor and an audio-amplifier helps to hear the muscle activity(ActiPatch® products 2018). An Electroneurogram (ENG) is used to visualize and record electrical activity of neurons by placing an electrode in the neural tissue. EMG and ENG are often performed at the same time help to detect presence, location, and extent of diseases related to nerve damage and destruction. An electroencephalogram (EEG) is a particular type of ENG in which several electrodes are placed around the head and the general activity of the brain is recorded. ERG measures the electrical activity of various cells in the retina in response to a light stimulus. It is clinically for the diagnosis and monitoring of various retinal diseases, detecting retained intraocular foreign bodies and evaluation of retinal toxicity with various drugs. ERGs use electrodes embedded in a corneal contact lens, which measure a summation of retinal electrical activity at the corneal surface. Electrogastrograph (EGG) records the electrical signals that travel through the stomach muscles and control the muscles' contractions.



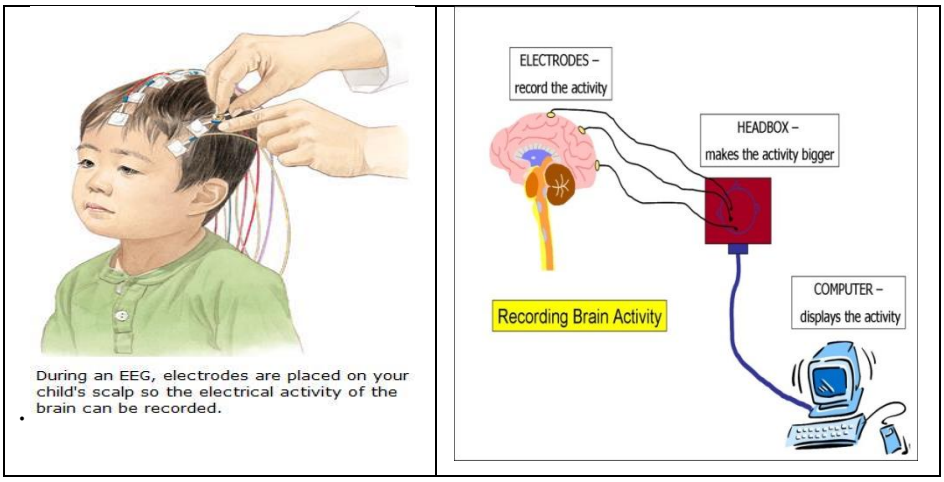
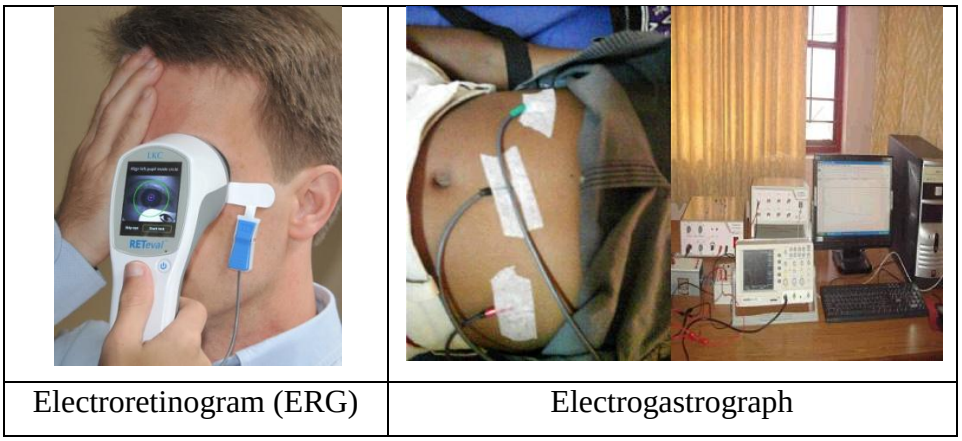


Figure 4: Picture depicting a new generation EMG/EEG systems Source:http://www.bcchildrens.ca/our-services/hospital-services/diagnostic-neurophysiology-eeg-emg/electroencephalography-(EEG)



Electroretinogram (ERG)	Electrogastrograph

Figure 5: Picture depicting a new generation ERG/EGG systems

Following are relevant US patents on electrophysiological medical devices

PAT. NO.	Title
9,681,814	Devices and methods for real-time denoising of electrocardiograms
9,649,042	Heart monitoring system usable with a smartphone or computer
9,572,499	Methods and systems for arrhythmia tracking and scoring
9,254,095	Electrocardiogram signal detection
9,026,202	Cardiac performance monitoring system for use with mobile communications devices
8,509,882	Heart monitoring system usable with a smartphone or computer
8,301,232	Wireless, ultrasonic personal health monitoring system

Imaging technologies

Imaging is an essential component of medical profession. Imaging technologies are often essential to medical diagnosis, and are typically the most complex equipment found in a hospital including, Magnetic resonance imaging (MRI), Nuclear Medicine, Positron Emission Tomography (PET), Projection Radiography such as X-rays and CT scans are some of the

medical devices. Newer and faster scanning techniques are developed with integration of computers, image reconstruction algorithms. Magnetic resonance imaging is an important non-invasive imaging technique used in radiology to examine internal body structures and diagnose a variety of disorders, such as strokes, tumors, aneurysms, spinal cord injuries, multiple sclerosis and eye or inner ear problems. MRI scanner is a medical application device of nuclear magnetic resonance (NMR).They use strong use a strong magnetic field and radio waves to generate images of parts of the body. The price of a clinical 1.5-tesla MRI scanner is estimated to be around US$1.4 million with its lifetime maintenance cost equivalent to its price. MRI scanners are significant sources of revenue for healthcare providers in western countries. MRI diagnosis cost is too high as evident from the cost and maintenance of equipment. Innovations in NMR or its medical application MRI or their components will be of great help to India in reducing cost of diagnosis, research costs and in chemical spectral analysis (Editor BCC Research 2007).

Following are relevant US patents on imaging technologies

PAT. NO.	Title
9,947,094	Medical image processing device, operation method and program
9,949,697	Imaging a body
9,949,700	Medical device approaches
9,952,157	Tissue imaging and visualization of lesions using reflectance and autofluorescence measurements
9,953,413	Identification and analysis of lesions in medical imaging

Sonography

Ultrasonic images, also known as sonograms. Sonography is a diagnostic imaging technique based on the application of ultrasound and is used to see internal body structures such as tendons, muscles, joints, blood vessels, and internal organs. It is widely used for examining pregnant women using ultrasound is called obstetric ultrasound. In sonography pulses of ultrasound waves of higher than audible frequencies are sent into tissue using a probe. Reflected echos of varying degrees of sound based on tissue type are recorded and displayed as an image to the operator. Based on the acoustic impedance different types of images can be formed in sonographic instruments. They can be used for understanding blood flow, tissue stiffness and motion, anatomy of organs. Ultrasound scanner offer several advantages over other prominent methods of medical imaging. They do not use harmful ionizing radiation, lower in cost, portable, can be used bedside and provide real time imaging. Various developmental techniques such as use of multisensory probes with the aid of computer image processing software, rotating or rocking the transducers improved the real-time moving images of the fetus (Kenneth Frazier 2016)

Following are relevant US patents on sonography

PAT. NO.	Title
9,949,717	Ultrasound detector and detecting device for optoacoustic or thermoacoustic imaging
9,947,090	Medical image dectection system and method
9,943,708	Automated control of micromanipulator arm while imaging

9,936,887	Method for evaluating blush in myocardial tissue

Endoscopes

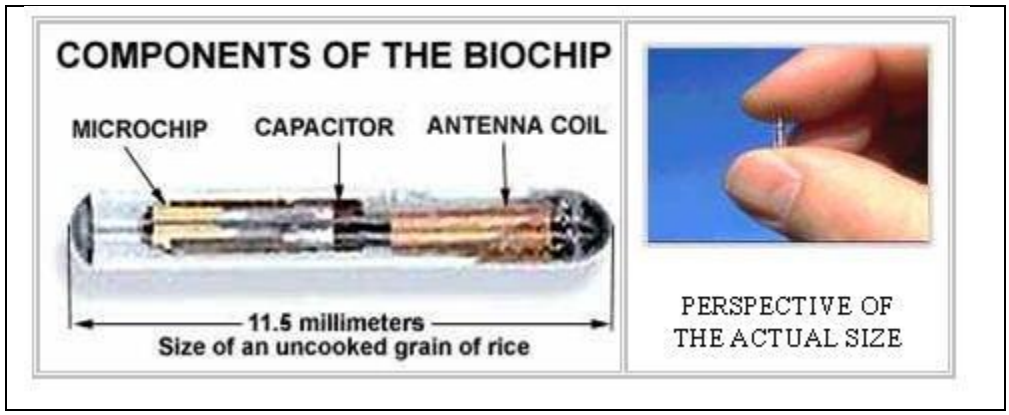
Wide range of flexible and versatile endoscopic medical electronic devices is developed with the development of miniature camera technology. With the help of these physicians can visualize various inaccessible areas of the gut, reproductive organs abdominal cavity and urinary tract. Capsule endoscopy is a new innovative technique. A video camera and transmitter are inserted into capsule and given to the patient. Such a capsule passes freely through the gut, transmitting color images to an external recording device (Norman. N. Rasmussen 1999)

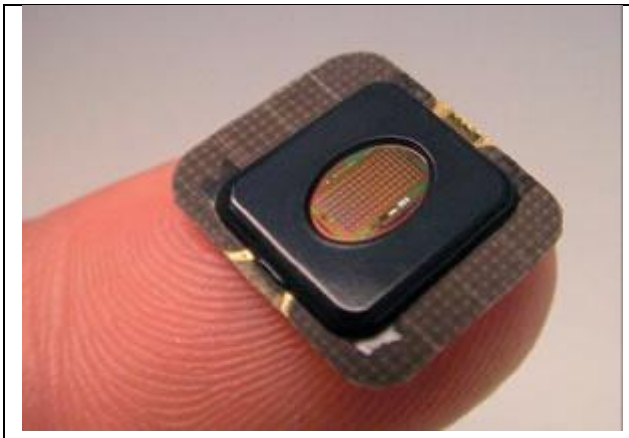
Biochips and biosensors

Bio-sensing is an important potential innovative area of new bioelectronics industry use microelectronic techniques and semiconductor components. Biochips and biosensors are considered to be the powerful tools for diagnostic, pharmaceutical, medical, modern biology research in the post-genomic era. They are products of applications of semiconductor and microelectronic industry and have a great potential for generating advanced technology and novel devices. Developments in miniaturization of sensor technology by use of micro electromechanical sensors (MEMS) technology have led to the size reduction of many biomedical instruments thereby increasing portability. The global market for biosensors and other bioelectronics is projected to grow from $6.1 billion in 2004 to $8.2 billion in 2009, at an AAGR (average annual growth rate) of about 6.3%. There is still lot of scope for improvements in bridging sensor signal processing and readout devices (Ali J 2016; Andrew McWilliams 2016).

Electroceuticals:

Electroceuticals are miniature electronic devices developed as innovative products for non-invasive treatments for diabetes, asthma, hypertension, arthritis, pain and even cancer. They attach to nerve bundles modulate the electrical impulses that are linked to specific organ functions , thereby triggering biochemical processes for pain management and provide targeted treatments with minimum side effects (Andrew Whelan 2017). North America is expected to account for the largest share of the electroceuticals and GSK is considered to be the leader in (Electroceutical research Editor 2016).





Biochip to detect microbial contamination

Microchip implant

Figure 6: Picture depicting a new generation biochips and electroceuticals.
Source: http://www.yuvaengineers.com/ bio-chips

Bioelectronic medical implants

Bioelectronic medicine involves implanting a small, battery-powered medical device in a patient's body using a minimal keyhole surgery and implants are designed to last for several years. They include cardiac defibrillators/pacemakers, deep brain neurostimulators, spinal cord stimulators, gastric stimulators, foot drop implants, cochlear implants, insulin pumps, retinal implants, implantable neural electrodes, muscle implants, and other implantable devices. Cardiac pacemakers provides a brief electric impulse that causes heart muscle cells to contract there by blood is sent to the rest of the body. Product improvements over a period of time lead to development of modern day the pocket watch size pacemakers which are totally implanted devices. Worldwide millions of patients have been benefitted by the use of cardiac pacemakers. Similarly functional electrical stimulation based muscle stimulators are developed for improvement in the quality of life for patients having difficulty in walking and treating paralyzed patients (Wise et al. 2004,Fionnuala Costello 2017)

Digital Hearing and Visual aids

Functional electrical stimulation based medical bioelectronics are being developed for impaired vision and hearing patients. Development of more efficient cost effective medical electronics such as digital cochlear implants and bionic eyes offers a great technical challenge and a business opportunity. Components of conventional cochlear implants are made up of metals which impose certain limitations as they conduct electricity. Development of Cochlear implants and bionic eyes made of soft flexible conductive polymers is an innovation made by scientists of center for implantable biopolymer bioelectronics.

Bionic eye is a new medical electronic device is close to being marketed uses a camera fitted to optical sun glasses and a processor that converts signals from analog to digital mode which is perceived by the body. This electronic device consists of a chip that collects and processes the information and transmits it to electrode lead inserted in the eye ball, which stimulates the cells of eye for visual perception. Devices that use electrical stimulation of the brain such as deep brain stimulators are developed to improve their quality of life of many Parkinson's patients. Such devices improve the quality of life of patients to help them to regain normal and near normal movement and mental function and offer many innovation opportunities (Biodesign institute 2018).

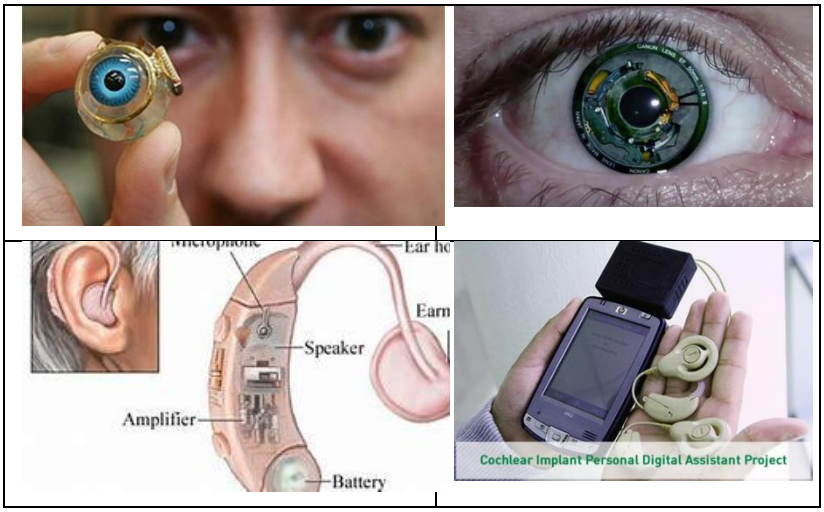


Figure 7: Picture depicting Images of new generation digital visual and hearing aids
Source: Google images

Discussion

There is a significant growth in healthcare industry in India and is estimated to be around USD 145 billion by 2018. Demographics, rising life expectancy, and growing public health awareness have contributed to a higher demand for medical care and a need for sophisticated hospital equipment. Medical devices sector plays a critical role in accessibility and affordability of quality healthcare service. It is estimated that 30-40% of capital costs of setting up a tertiary care hospital is attributed to medical technology and medical devices and diagnostics contribute approximately 20%-25% to the cost of medical services (Charu shegal 2016). According to market research report the global medical devices and technology market is expected to grow to USD 520 billion by 2020.The Indian medical device sector market is among the top twenty in the world by market size and is considered as Asia's fourth largest market valued at worth approximately USD 5.5 Billion in 2015 and is expected to exceed $7 billion by the end of 2020 with 15% CAGR. However, the per capita spending on medical devices in India is relatively low and is significantly behind developed economies l US and Europe. This represents a great opportunity for India to capture contract research market and global medical electronic device market by supply of high technology, specialized medical equipment, products, and systems (, Bethan, Grylls 2018 Thonte S.S. et al 2016).

India's manufacturing ability for many cost effective industrial products such a semi conductors is well established. But still at present domestic companies are largely engaged in manufacturing low-end products for local and international market. We are still highly dependent on imported medical equipment and devices which account for almost 70% of sale market. Although it is estimated that there are around over 750 medical device manufacturers, only a few of them make good turnover (Eli tech group 2017). Providing an affordable and quality healthcare is a major challenge in the country Imbalance between current demand and supply provides a significant opportunity and rationale for manufacturing medical devices in India. Limited research funds, innovations and technological developments and demand for quality health care are some of the causes for import dependence. Indian medical device industry has to reduce the dependence on imports and produce quality affordable high end medical .In view of great demand for medical electronics worldwide we must identify key research and technological factors for growth and explore the possibilities to capture the export market. The Government of India's 'Make in India'

is a very good essential initiative for innovations, indigenous medical device industry manufacturing.

Conclusion

The field of bioelectronics is growing at an exponential rate innovations are possible as indicated by market survey reports, literature and patent search. Commercialization of bioelectronics will require expertise and innovations from the biomedical and electronics academia, research institutions and industry. Indian has established its manufacturing ability in semiconductors and traditionally focused on information and communications technology applications and products to provide significant revenues to the national exchequer. Through bioelectronics and biomedical applications semiconductor industry can further add substantial value. Export potential of revenue generating areas of electronic market such as semiconductors, bio sensors, bio instrumentation and medical electronics has to be explored in a coordinated and integrated manner to firmly establish India as a leader in this high impact area of bioelectronics manufacturing, research and development. Accordingly skill development programs, research funding, innovations, entrepreneurship and manufacturing, biomedical device industry need be given special encouragement and support to harness.

References:

ActiPatch® products, BioElectronics Corporation available at http://www.actipatch.in March 2018

Ali J, Najeeb J, Ali MA, Aslam MF, Raza A (2017) Biosensors: Their Fundamentals, Designs, Types and Most Recent Impactful Applications: A Review. J Biosens Bioelectron 8: 235. doi: 10.4172/2155-6210.1000235, November 24, 2016

Alyssa Danigelis, Body Bioelectronics: 5 Technologies that Could Flex with YouLive Science Contributor https://www.livescience.com/53806-flexible-bioelectronics-innovations.html February, 2016

Andrew McWilliams, https://www.bccresearch.com/market-research/biotechnology/ BIO039B. html, April 2016

Andrew Whelan, Bio Electronics changing the way people heal and stop pain, Binghamton University News letter, https://www.binghamton.edu/research/innovation/econdev/biel.html

Aparna Mishra, 5 Hardware Startups That Are Changing he Healthtech Game in India, available at https://inc42.com/startups/hardware-healthtech-startups, November 2016

Bethan Grylls, Bringing on bioelectronics available at http://www.newelectronics.co.uk/article-images/169283/P21-22.pdf March 2018

Biodesign institute, News on "Vision: Integrated sensor systems with global impact" available at https://biodesign.asu.edu/bioelectronics-and-biosensors, March 2018

Burch & DePasquale, A history of electrocardiography. San Francisco Norman, August 1990.

Charu Sehgal,Medical Devices Making in India - A Leap for Indian Healthcare,Deloitte article available at http://www.nathealthindia.org/pdf/Deloitte_NATHEALTH_Medical%20Devices%20%20Making%20in%20India.pdf march 2016.

Dave Fornvell, Advances in ECG Technology available at https://www.dicardiology.com/ article/advances-ecg-technology, September, August 2015

December 2017

Editor, Electroceuticals Medicine market report, https:// www.marketsandmarkets.com /Market-Reports/electroceutical-market-222053956.html, June2016

Editor, Global Market for Medical Imaging Equipment Worth $11.4 Billion by 2012 Says BCC Research Study, Drug Week, 2007.

Eli tech group, Bioelectronics: Future of Medical Technology www.elitechgroup.com/ category/news/product-news, July 2017

Fionnuala Costello, Exciting opportunities for implants and bioelectronics, New article https://innovateuk.blog.gov.uk/2017/10/09/exciting-opportunities-for-implants-and-bioelectronics/ October 2017

Grand view research report, available at https://www.grandviewresearch.com/ industry-analysis/stethoscopes-market, Nov, 2017

GSK research team, Bioelectronics research, https://www.gsk.com/en-gb/research/what-we-are-working-on/bioelectronics-research/ March 2018

Htf market report, Asia-Pacific Bio-Electronic Market Report, Bio-Electronic Market by Leading Key Players, https://factsweek.com/653506/bio-electronic-market-by-leading-key-players-, April 2018

José R. Banegas et al., Relationship between Clinic and Ambulatory Blood-Pressure Measurements and Mortality, New England Journal of Medicine. DOI: 10.1056/NEJMoa1712231, April**.** 2018

Kenneth Frazier, Technology frontiers: bioelectronic medicine, the epicenter of the future: where healthcare, technology & science converge, CEWIT Newsletter_JULY2016

Nic Lempriere-Hogg, Bioelectronic Monitoring and the Future of Underwriting, A report from RGA Reinsurance Company, August 2017

Norman. N. Rasmussen, Picture Control: The Electron Microscope and the Transformation of Biology in America, 1940-1960, Stanford University Press, August 1999.

Omprakash Gadgeppa , Smart bioelectronics the future is electric, article available at: https://www.researchgate.net/publication/299391689, April 2016

Thonte S.S. et al., College Smart bioelectronics :the future is electric, https://www.researchgate.net /publication/299391689 march 2016

Wise KD., Anderson DJ., Hetke JF, Kipke DR. and Najafi K., Wireless implantable microsystems: high-density electronic interfaces to the nervous system, Proc IEEE, 92, 76-97, January 2004.